REMARKS

Claims 1, 2 and 4-77 are pending. Claims 1, 2, 4-33, 35-43 and 75-77 are under examination. Claims 1, 16, 32 and 75-77 have been amended. Support for the amendments can be found throughout the specification and the claims as filed. In particular, support for the amendments to claims 1, 16, 32 and 75-77 can be found, for example, on page 17, lines 16-20, page 18, lines 14-21, and page 38, line 27, to page 40, line 23. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

Rejection Under 35 U.S.C. § 101

The rejection of claims 1, 2, 4-33, 35-43 and 75-77 under 35 U.S.C. § 101 as allegedly being directed to non-statutory subject matter is respectfully traversed. Applicants respectfully submit that claims 1, 2, 4-33, 35-43 and 75-77 are directed to statutory subject matter.

In re Bilski, 545 F.3d 943, (Fed. Cir. 2008) held that a process claim defines patentable subject matter if "(1) it is tied to a particular machine or apparatus, or (2) it transforms a particular article to a different state or thing." *Id.* at 954, 956 (*citing Gottschalk v. Benson*, 409 U.S. 63, 70 (1972)). Applicants respectfully submit that the claimed invention meets either or both branches of this "machine-or-transformation" test articulated by the *Bilski* court.

The Examiner asserts that the claimed invention is not limited to a particular apparatus or machine. The Examiner further asserts that the claims should require use of a machine within the steps of the claim or require transformation of an article to a different state or thing.

The question before the *Bilski* court was whether the claimed process recited a fundamental principle and, if so, whether it would pre-empt substantially all uses of that fundamental principle if allowed (see *Biski*, fn 5 at 952, defining a fundamental principle to mean laws of nature, natural phenomena and abstract ideas). *Id.* at 954. The claims in issue were directed to a business method of hedging risk in the field of commodities trading. *Id.* at 949. The court held that the claimed method was not directed to patent-eligible subject matter because there was no transformation of an article into a different state or thing.

In arriving at this conclusion, the court analyzed Federal Circuit precedent with respect to the transformation test to clarify "what sorts of things constitute 'articles' such that their transformation is sufficient to impart patent-eligibility under § 101." *Id* at 962. Recognizing that "[t]he raw materials of many information-age processes . . . are electronic signals and electronically manipulated data" and addressing "[w]hich, if any, of these processes qualify as a transformation or reduction of an article into a different state or thing" (*Id.* at 962) the court concluded:

> So long as the claimed process is limited to a practical application of a fundamental principle to transform specific data, and the claim is limited to a visual depiction that represents specific physical objects or substances, there is no danger that the scope of the claim would wholly pre-empt all uses of the principle.

Id. at 963 (emphasis added).

Relying on the mixed results in *Abele*, (*In re Abele*, 684 F.2d 902 (CCPA 1982), the *Bilski* court noted that a claim directed to a process of graphically displaying variances of data from average values was held unpatentable because the claim did not specify any particular type or nature of data, how or where the data was obtained or what it represented. In contrast, a dependent claim directed to X-ray attenuation data produced by computer tomography was found to be statutory subject matter because:

> This data clearly represented physical and tangible objects, namely the structure of bones, organs, and other body tissues. Thus, the transformation of that raw data into a particular visual depiction of a physical object on a display was sufficient to render that more narrowly-claimed process patent-eligible.

Bilski 545 F.3d at 962-63 (*citing Abele*, 684 F.2d at 908-09).

Bilski further clarified that electronic transformation of data is sufficient to render a process claim patent eligible subject matter when the court stated:

> We further note for clarity that the electronic transformation of the data itself into a visual depiction in *Abele* was sufficient; the claim was not required to involve any transformation of the underlying physical object that the data represented. We believe this is faithful to the concern the Supreme Court articulated as the basis for the machine-or-transformation test, namely the prevention of pre-emption of fundamental principles.

Id. at 963 (emphasis added).

Thus, *Bilski* found that, when properly applied to electronic signals and electronically manipulated data, the transformation branch of the machine-or-transformation test does not require transformation of a underlying physical object the data may represent. Rather, the transformation branch is satisfied when electronic data is transformed into a visual depiction. Applicants respectfully point out that the claimed invention satisfies this branch of the test.

Independent claims 1, 2, 4-33, 35-43 and 75-77, as amended, recite providing a visual output to a user. Therefore, the claim "transforms specific data . . . to a visual depiction that represents specific physical objects or substances [and] there is no danger that the scope of the claim would wholly pre-empt all uses of the principle. *Bilski*, 545 F.3d at 963 (*supra*). Accordingly, independent claims 1, 2, 4-33, 35-43 and 75-77 are patent-eligible subject matter because they satisfy the transformation branch of the machine-or-transformation test articulated by the Supreme Court and clarified in *Bilski*. Additionally, independent claims 1, 2, 4-33, 35-43 and 75-77, as amended, recite a computer, thereby requiring the use of a machine within the steps of the claim. Although not required to satisfy both alternatives of the machine-or-transformation test, nevertheless, independent claims 1, 2, 4-33, 35-43 and 75-77 also satisfy the alternative machine implementation branch of the test.

In light of the above remarks and amendments, Applicants submit that the claimed invention falls within statutory patentable subject matter. The claims meet the transformation branch of the machine-or-transformation test articulated in *Bilski* because it transforms electronic data to a visual depiction. While not required, the claims also meet the machine implementation branch of the test because the claimed method is tied to a computer. Accordingly, Applicants respectfully request that this ground of rejection be withdrawn.

Rejections Under 35 U.S.C. § 102

The rejection of claims 1, 2, 4-33, 35-43 and 75-77 under 35 U.S.C. § 102(b) as allegedly anticipated by Rine et al., U.S. Patent No. 5,777,888, is respectfully traversed. Applicants respectfully maintain, for the reasons of record, that Rine et al. does not anticipate the claims.

As discussed in the previous response, each of independent claims 1, 16, 32 and 75, and amended claims 76 and 77, recite that each data integration map comprises a value set containing

two or more different types of data elements wherein, the different types of data elements are integrated into each of the value sets. Applicants respectfully maintain that Rine et al. fails to describe such an integration of different types of data elements. As taught in the specification, a "data integration map" refers to an indexed set of data elements corresponding to components that describe the interactions, interrelations, and interdependencies of the components included within the biochemical or constituent system (page 16, lines 13-18). As additionally taught in the specification, a "value set" refers to a set of two or more types of data elements that characterize a component of a biochemical system (page 17, lines 26-29). As noted above and in the previous response, the claims explicitly recite that the value set contains "two or more different types of data elements" and that the two or more different types of data elements are integrated into each of the value sets. The specification additionally teaches that a "data element" refers to a value or other analytical representation of factual information that describes a characteristic or a physicochemical property of a biochemical system or a component of a biochemical system (page 18, lines 9-14).

The specification further teaches that a "value set can contain one or more of a particular type of data element. For example, a value set of a system component that interacts with multiple molecules can include data elements characterizing a physical interaction corresponding to each interacting molecule. A value set additionally can contain one or more different types of data elements. For example, a value set of a system component can include data elements characterizing one or more physical interactions, an mRNA expression level, polypeptide expression level, activity, system phenotype and growth rate" page 17, line 29, to page 18, line 8). Thus, it is clear that the data integration map as recited in the claims comprises value sets and therefore two or more different types of data elements. Moreover, as discussed above and in the previous response, the different types of data elements integrated into each value set can include, for example, nucleic acid expression, protein expression, polypeptide-polypeptide interaction, nucleic acid-polypeptide interaction, metabolite abundance and growth rate. The claimed value sets integrate two or more of these different types of data elements into a single value set.

As discussed in the previous response, Rine et al. fails to describe a data integration map comprising value sets containing two or more different types of data elements wherein the two or

more different types of data elements are integrated into each of the value sets. Referring to Rine et al., this reference, at best, describes methods of screening and comparing information obtained using an array but no teaching of the claimed methods. "The present invention combines these [artificial intelligence and *in vitro* or cell culture-based methods] approaches to provide an in vitro or cell culture-based analysis of systemic response patterns. In particular, the invention involves sophisticated methods for generating and analyzing highly informative stimulus-systemic repression and activation response patterns" (Rine et al., col. 1, lines 58-63). Rine et al. further describes:

> FIG. 3 provides a schematic representation of a stimulated physical matrix. The stimulated physical matrix 310 comprises an ordered array of units having X and Y coordinates. While FIG. 3 depicts four illustrative units 312, in practice, the matrix will typically have about a hundred or more units. The units are generally a region of a solid substrate such as a two-dimensional portion of the surface of a silicon-based wafer, a well of a microtiter plate, etc. Each unit confines either a different responder 314 of a living thing or a probe 316 corresponding to such a different responder and, an identifier 318 for the responder or probe. Generally, all the units of a given matrix will employ a responder or all will have a probe. Further, for most convenient detection and data processing, all the units of a given matrix generally use the same identifier.
>
> The living thing (or, organism) is provided a stimulus capable of repressing the responders 314 of a plurality of the units 312 and the identifier 318 provides a physical signal corresponding to the repression of such different responder 314. Responses, usually cellular, to a wide variety of stimuli may be monitored. Examples of stimuli include candidate pharmacological agents, suspected pathogenic agents, transfected nucleic acids, radiative energy, etc. The stimulus induces the repression of a plurality of the responders of the matrix, relative to their pre-stimulus state of induction, as measured by the pre-stimulus output signal at the corresponding unit. Typically, the stimulus provides a complex response pattern of repression, silence and induction across the matrix. The response profile reflects the cells' transcriptional adjustments to maintain homeostasis in the presence of the drug. Hence, while a wide variety of stimuli may be evaluated, it is important to adjust the incubation conditions (e.g. stimulus intensity, exposure time, etc.) to preclude cellular stress, and hence insure the measurements of pharmaceutically relevant response profiles. The arrays may comprise the organism's entire repertoire of responders which may be genes, gene regulatory elements, gene transcripts ***or*** gene translates (proteins), ***or*** a predetermined functional class or subset of the organism's entire repertoire. By incorporating at least 0.5%, preferably at least 5%, more preferably at least half, most preferably essentially all the responders (***e.g. gene regulatory regions***) of the organism, an in vitro or cell culture model of the organism (e.g. animal) may be obtained. In a preferred embodiments, the array comprises a sufficient

> ensemble of responders so as to model the systemic response of the organism and to deduce the action of a stimulus regardless of its mechanism of action. [col. 3, line 28, to col. 4, line 8; emphasis added]

Thus, Rine et al. clearly describes an array suitable for measuring cellular responses to a stimulus. Rine et al. goes on to describe:

> The nature of the linkage **320** between the responder and identifier will vary with the application of the matrix. As examples: each unit of a matrix reporting on gene expression might confine a cell having a construct of a reporter gene operatively joined to a different transcriptional promoter; alternatively, each unit of a matrix reporting on gene expression might confine a different oligonucleotide probe capable of hybridizing with a corresponding different reporter transcript; each unit of a matrix reporting on DNA-protein interaction might confine a cell having a first construct of a reporter gene operatively joined to a targeted transcription factor binding site and a second hybrid construct encoding a transcription activation domain fused to a different structural gene (a one-dimensional one-hybrid system matrix); each unit of a matrix reporting on protein-protein interactions might confine a cell having a first construct of a reporter gene operatively joined to a targeted transcription factor binding site, a second hybrid construct encoding a transcription activation domain fused to a different constitutionally expressed gene and a third construct encoding a DNA-binding domain fused to yet a different constitutionally expressed gene (a two-dimensional two-hybrid system matrix). [col. 4, lines 9-30]

Thus, it is clear from this context of Rine et al. that a matrix contains units each of which is designed to assay a particular activity, for example, gene expression using a reporter gene or oligonucleotide probe, DNA-protein interactions, or protein-protein interactions using known respective assays for such methods. However, each matrix itself is used to determine a single type of information such as gene expression, protein-DNA interactions or protein-protein interactions. Thus, it is clear from the description of Rine et al., as discussed above, that a "stimulated physical matrix" is not a data integration map, as asserted in the Office Action on page 4. To the contrary, Rine et al. provides no teaching of a data integration map comprising value sets containing two or more different types of data elements wherein the two or more different types of data elements are integrated into each of the value sets.

The Office Action on page 4 characterizes the teachings of Rine et al. as follows:

> Rine et al. disclose constructing a stimulated physical matrix (data integration map which is a physical interaction map), detecting a physical signal (value) at each unit of the physical matrix and storing the output signal matrix data with X

> and Y coordinates of the corresponding physical matrix unit (i.e. value sets), and repeating this procedure including constructing a stimulated physical matrix for a plurality of stimuli to form a database (col. 2, lines 4-15) and comparing the output signal matrix to an output signal matrix database (other matrices) which represents producing and comparing two or more data integration maps obtained under different conditions. [emphasis added]

As discussed above and further below, Applicants respectfully submit that various terms of the claims (underlined above) have been asserted to be described in Rine et al., but the interpretation set forth in the Office Action purportedly supporting an interpretation of Rine et al. to describe these terms is clearly inconsistent with how one skilled in the art would understand the meaning of these terms as recited in the claims and taught in the specification. For example, as discussed above, it appears that the "stimulated physical matrix" of Rine et al. has been interpreted to be a data integration map, as recited in the claims. However, such an interpretation of the single type of data being measured with the stimulated physical matrix of Rine et al. clearly is no description of a data integration map comprising value sets containing two or more different types of data elements wherein the two or more different types of data elements are integrated into each of the value sets. This interpretation is corroborated by Figure 6 of Rine et al., which describes generating a gene reporter matrix. Starting in column 11, Rine et al. describes how to generate a gene reporter matrix.

> To generate a genome reporter matrix **610** a set of lacZ fusions are constructed to a comprehensive set of yeast genes... The fusions are arrayed onto a grid separating distinct fusions into units having defined X-Y coordinates... An index table **614** is established relating each gene in the matrix to the X-Y coordinate of the fusion construct for that gene.
>
> The basal response determination function **616**, is performed by measuring the basal response of each cell in the matrix under a variety of physical conditions, such as temperature and pH, medium, and osmolarity. This information is indexed against the matrix to form the reference response profile set **618** that will be used to determine the response of each reporter to any milieu in which a stimulus may be provided.
>
> The compound treatment function **620** is performed by contacting each unit of the matrix with a test compound. Generally, a copy of the entire matrix is transferred to fresh medium containing the first compound of interest and the response is obtained for the entire matrix. In a reference subtraction function **622**, the appropriate reference response profile is subtracted from the response profile, and the difference stored in the knowledge base as the first chemical response profile

> **624**. Alternatively, the response profile is divided by the appropriate reference profile to yield an induction ratio. The process is repeated for compounds or mixtures of compounds 2 through N.
>
> The gene mutation function **626** determines the response of the matrix to loss of function of each protein or gene or RNA in the cell introducing a dominant allele of a gene to each reporter cell, and determining the response of the reporter as a function of the mutation... The data obtained identifies genetic response profiles 1-N **628**...
>
> These data are subject to a sorting function **630** which sorts by individual gene response to determine the specificity of each gene to a particular stimulus... A gene regulation function **634** is then used to construct tables of regulation **634**, **636** identifying which cells of the matrix respond to which mutation in an indexed gene, and which mutations affect which cells of the matrix.
>
> The unknown stimulus matrix screen function **636**, sequentially tests new chemicals or unknown compounds or unknown mixtures to identify output response profiles **642**. [col. 11, line 1, to col. 12, line 3]

Thus, it is clear that, while various stimuli are being tested, the same reporter is being analyzed. In other words, only a single type of data is being determined on a given matrix, albeit under different conditions. Therefore, it is clear that a stimulated physical matrix, which measures a single type of data, cannot be a data integration map comprising value sets containing two or more different types of data elements wherein the two or more different types of data elements are integrated into each of the value sets.

Referring again to the passage from the Office Action recited above, it is asserted that Rine et al. discloses "detecting a physical signal (value) at each unit of the physical matrix and storing the output signal matrix data with X and Y coordinates of the corresponding physical matrix unit (i.e. value sets)." Based on this passage, it appears that "X and Y coordinates" have been interpreted as "value sets." However, it is clear from the description in Rine et al. that "X and Y coordinates" merely refer to the position on the array. "The stimulated physical matrices comprise an ordered array of units having X and Y coordinates" (col. 2, ln, 30-31; see also Figure 3). It is clear that the X and Y coordinate "values" are completely arbitrary based on the position of a given unit on the array (physical matrix). In contrast and as discussed above, a "value set" refers to a set of two or more types of data elements that characterize a component of a biochemical system. Clearly the arbitrary placement of an element on a matrix, thereby assigning that element an X and Y coordinate, provides no teaching of a value set of two or more

types of data elements that characterize a component of a biochemical system, as taught in the specification (page 17, lines 26-29).

In several places in the Office Action (for example, pages 6, 8, 9, and 10), passages from Rine et al. are referred to as describing that "a response profile (i.e. value set) incorporating preferably all the responders of the organism to obtain an in vitro or cell culture model, including units reporting gene expression, DNA-protein interaction, and protein-protein interaction (col. 3, last paragraph to col. 4, second paragraph) which represent at least three different types of data elements integrated into value sets" (page 6). However, this passage from Rine et al. is quoted above in context and reiterated here, "[T]he arrays may comprise the organism's entire repertoire of responders which may be genes, gene regulatory elements, gene transcripts ***or*** gene translates (proteins), ***or*** a predetermined functional class or subset of the organism's entire repertoire." Thus, it is clear that, when this passage of Rine et al. is viewed in context, these responders are alternatives for measuring the activity of a given stimulus. As discussed above, any given matrix is measuring one type of responder, and Rine et al. provides no teaching of integrating two or more types of data elements into value sets.

As discussed in the previous response, "[A] claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." M.P.E.P. § 2131 (quoting *Verdegaal Bros. v. Union Oil Co.* of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987)) (emphasis added). A rejection under § 102 is proper only when the claimed subject matter is identically described or disclosed in the prior art. *In re Arkley*, 455 F.2d 586, 587 (CCPA 1972); M.P.E.P. § 706.02.

Applicants respectfully maintain, for the reasons of record and as discussed above, that Rine et al. does not teach each and every element of the claims, as required to anticipate the claims. Absent such a teaching, Applicants respectfully submit that the claimed methods are novel over Rine et al. Accordingly, Applicants respectfully request that this rejection be withdrawn.

The rejection of claims 1, 2, 4-33, 35-43 and 75-77 under 35 U.S.C. § 102(e) as allegedly anticipated by Thalhammer-Reyero, U.S. publication 2005/0273305, is respectfully traversed.

Applicants respectfully maintain, for the reasons of record, that the claimed methods are novel over Thalhammer-Reyero.

The Office Action refers to a number of places in Thalhammer-Reyero as alleged support for various aspects of Applicants' claimed methods. It is again noted for the record that Thalhammer-Reyero was filed December 5, 2004, well after the filing date of the present application of November 13, 2001. It is further noted for the record that certain claims of Thalhammer-Reyero were copied from the publication of the present application. Applicants refer to Exhibit 1 filed with Applicants' response on November 9, 2007, which is a copy of a Preliminary Amendment filed July 14, 2005, in the 11/004,500 application of Thalhammer-Reyero. On page 12 of the Preliminary Amendment, it is explicitly stated that "claims 253-264" were copied "from 20030130798 published 07/10/2003," which is the publication corresponding to the present application. As previously noted on the record and reiterated herewith, no support was provided in the Preliminary Amendment for any of the new claims, including claims 253-264 copied from the present application. The Preliminary Amendment additionally states that "new claims 395-419 are added to distinctly claim particular embodiments of the elected invention." However, again no support is provided for these new claims. Thus, the record of Thalhammer-Reyero provides no support for new claims 259-262 or claims 412-414. Applicants respectfully maintain that none of these claims is supported by the original disclosure of Thalhammer-Reyero and, given their later filing date, cannot constitute prior art against Applicants' claimed methods.

Turning to the current Office Action, there continues to be reference to claims 259-262 and 412-414 as support in Thalhammer-Reyero for alleged teachings of Applicants' claimed methods (see Office Action pp. 12-13). To counter Applicants' position of record, the Office Action states (paragraph bridging pp. 13-14) "Applicant argues that the Examiner's statement that claim 259 is found in the originally filed specification lacks support and is conclusory. This statement is found unpersuasive as support can be found, for example, in Thalhammer-Reyero paragraphs 0016, 0070, 0021, 0082, 0102, 0149, 0589 and Figures, such as, 36a and b" (emphasis added). Applicants will discuss the alleged support provided by these passages in more detail below. Nevertheless, Applicants note for the record that a search of the Thalhammer-Reyero publication for claim terms such as "data integration map" and "value set"

provides the first "hit" of such terms in claim 259. Therefore, no teaching of these terms can be found in the specification of Thalhammer-Reyero, substantiating Applicants' position that claim 259 can, at best, be afforded a priority date of the filing date of Thalhammer-Reyero, December 5, 2004, well after Applicants' priority date of November 13, 2001.

With respect to the passages referenced in the Office Action as allegedly supporting claim 259, it is respectfully submitted that no such support for claim 259 can be found in these or any passages from Thalhammer-Reyero. Referring to paragraph [0016]:

> [0016] Some process industries use large-scale cultivation of microorganisms or mammalian cells, which are extreme cases in terms of complexity when considering those cells as the individual manufacturing plants involved in complex chemical synthesis. Microorganisms are the preferable systems for producing natural substances that have a multitude of uses, such as drugs, foods, additives, biodetergents, biopolymers, and other new and raw materials. Mammalian cells are the preferable systems for producing potent active substances for therapeutic and diagnostic uses. The ultimate level of complexity is using a whole animal as the live factory for continuous production for important secreted proteins. However, the current systems only monitor very general types of phenomena, such as gas pressure, pH, and in some occasions, the concentration of some product that correlates with cell growth or production. For example, for controlling the production of a particular secreted protein that is produced in very low amounts in relation to other proteins, the total protein amount of protein is measured, which is a very poor indicator of how much of the desired protein is produced. Complex mixtures of chemical reactions could be finely controlled externally by modifying the types and amounts of inputs added, if one could predict what will happen by adding those inputs, which requires a good knowledge and a model of such system of reactions. This is particularly the case with biological cellular systems that have very sophisticated methods to transduce the signals provided by ligands in their external environment to the interior of the cell, resulting in the execution of specific functions. Such detailed and accessible mechanistic models of those pathways of reactions are not currently used for monitoring and control systems, but would be highly desirable. This invention provides the system and methods that allows scientists to visually build detailed mechanistic models of the complex systems involved, and to further develop and use inference methods to integrate the simulation of those Virtual Models with inputs from monitoring devices to allow for the intelligent control of the operation of the complex system.

Paragraph [0016] of Thalhammer-Reyero, at best, describes bioproduction systems and modeling of such systems but no teaching that appears to relate to claim 259 of Thalhammer-Reyero or Applicants' claimed methods. Applicants respectfully request that the Examiner provide

guidance on what aspect of paragraph [0016] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to paragraph [0070]:

> [0070] The system provides a graphical computation and control language, where the objects communicate through the links established between them. Some of those linkages are built in within the composite prebuilt building blocks, while the modeler establishes other links between appropriate components from different building blocks. Other information, such as the name, description, references, or the values of parameters specific for each component are entered by the modeler. Variables in this system are themselves objects, and maybe of two major classes: a) one-valued variables have only one value, which may be either provided during a simulation by a simulation formula or procedure, or inferred by any other means, such as rules or general formulas defined by the modeler; and b) two-valued variables have two values: the simulated-value as before, and the measured-value is provided in real time through an external sensor mapped to said variable. The one-valued variables are used by default because of their smaller footprint, and their values are provided by default by generic simulation formulas that are specific for each class of variable. However, the modeler can replace them with the equivalent subclasses of two-valued variables for each instance of a component where the variable is mapped to an external sensor, and when both the measured valued and the simulated value of such variable is desired. The modeler can also write specific formulas for any desired instance of a variable, which then overrides the default generic formulas. It is possible, through any of the inference mechanisms to compare the measured value and the simulated-value, either the current values or the values mapped at some time point in the past, since the system is able to keep a time-stamped history of both types of values, and take specified actions when the inference criteria are met, such as: causing a valve for a component feed to be more or less open or closed, or activating or deactivating whole branches of the model pathways being simulated. Such actions can alternatively be invoked as a result of comparing either the measured-value or the simulated-value to any predefined constant value or range of values, or the value of any other variable or parameter in the system. Or the action or set of actions could result from inferences involving any number of comparisons between measured-values or simulated-values for any number of variables, or any number of parameters, or any predefined constant values.

Paragraph [0070] of Thalhammer-Reyero, at best, describes a production system model (see also preceding paragraph [0069]) but no teaching relating to claim 259 of Thalhammer-Reyero or Applicants' claimed methods. It is noted that this passage does recite the term "value," but it is clear in the context of the paragraph that such "values" are not "value sets" as recited in the claims (see also discussion above). Applicants respectfully request that the Examiner provide

guidance on what aspect of paragraph [0070] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to paragraph [0021]:

> [0021] The modeled system's behavior is defined by mathematical components, represented by a set of model differential and algebraic equations that provide the values of the system's variables and describe their behavior, together with the set of associated parameters that control the behavior of the variables and the system as a whole. The system's variables and parameters are embedded and distributed throughout the system of connected structures, encapsulated within the subcomponents that define the system's architecture. The model can then be viewed as a set of embedded block diagram representations of the underlying equations that can be used for dynamic numerical simulation and prediction of the effects of perturbations on the system, and to ask what-if type questions.

Paragraph [0021], at best, appears to provide an overview of the system model of Thalhammer-Reyero but no teaching relating to claim 259 or Applicants' claimed methods. Applicants respectfully request that the Examiner provide guidance on what aspect of paragraph [0021] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to paragraph [0082]:

> [0082] Depending on the application requirements, the interfaces may provide bridges to Supervisory Control and Data Acquisition (SCADA) systems (such as the HP's RTAP SCADA or others), Distributed Control Systems (DCS) (such as Honeywell TDC3000 DCS or others) or Programmable Logic Controllers (PLCs) (such as Allen-Bradley's PLC3/PLC5 families, or others), with the adequate protocol drivers, as well as to relational databases, object-oriented databases, ASCII files, as well as to a number of other connectivity applications, allowing the program to send or receive values over said interface. The program (**114**) and the interfaces (**120, 130**) are separate processes, which may be located on one or more host computers. In the later case, a communications link, such as a TCP/IP or DECnet protocols based link and port, is required. The program can also use various interfaces simultaneously, linked to different types of devices. The interface serves as a bridge between selected variables embedded in the objects of the Virtual Models and their corresponding mappings in one or more external systems. Functions defined in the interface can be invoked by remote procedure calls (RPCs) defined in the program, and viceversa.

Paragraph [0082], at best, describes the computer system for the model described in Thalhammer-Reyero but no teaching relating to claim 259 or Applicants' claimed methods. Applicants respectfully request that the Examiner provide guidance on what aspect of paragraph [0082] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to paragraph [0102]:

> [0102] In the current implementation of this invention, the variables embedded in the model that are set to get values from the sensors (such as the concentrations of the corresponding bioPools) inherit their properties from two parent classes: a class of float-variable and a class of interface-data-service. One of the attributes of the later class is Interface, which value defines the interface that will provide the current value for such variable. The value for such variable, the same as for any other variable in this system, can be set to be evaluated at set intervals, or it can be set to its value having a value that expire after a set validity interval. When the inference engine seeks the value of said variable, either at the preset update intervals or when such value is needed but has has [sic] expired, a request if set to the specified interface to provide a value. Such variables are registered in the interface. After the interface is set-up, when the start_interface function is called by the program and the connection established between the interface (**107**) process and the computer program (**115**) process, the functions executed by the interface comprise: initialize_context (initializes the connection between the program and the interface), pause_context, resume_context, shutdown_context, receive_registration (called when the program seeks to map for the first time a variable to an external data point); receive_deregistration, poll for data (checks periodically which registered variables need updating, retrieved data values available, packages the data into the data structure used by the return functions, and sends the data back to the program (**115**); get_data (called when the program requests data service for one or more registered variables); set_data (called when the program executes one or more set actions within a rule or procedure, it sends a request to the interface to set the external data point to which the registered variable is mapped, it also may call interface return functions to change the value of the registered variable after its corresponding value in the external system has been changed). The interfaces perform also many other functions related to passing objects and messages, checking data types, and several other API functions. [emphasis added]

Paragraph [0102], at best, describes "variables embedded in the model that are set to get values from the sensors." It is noted that this passage discusses that the value of the variable can be set at time intervals or for a given period of time (see emphasis above). However, such a description in no way teaches a "value set" as recited in the claims (see discussion above). Applicants

respectfully request that the Examiner provide guidance on what aspect of paragraph [0102] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to paragraph [0149]:

> [0149] Life and growth depends upon closed cycles of mutually dependent interactions. In a constant environment, the proportions of the various constituents settle down to constant values and a steady-state is reached. The steady-state correspond to an optimum state, since the lack of such balanced state would lead to rate-limiting steps. When the environment changes, those proportions move towards new values to achieve again optimum growth in the new environment. The principle underlying this system's dynamic modeling is the network of a combination of state and dependent variables, encapsulated within the structure of the bioObjects contained in the specified bioModel. The bioObjects provided are programmed by default for steady-state modeling. A dynamic simulation is initiated after the introduction of desired perturbations or initial conditions by the user, and the input data initiates a forward chaining, which involves both control and data flow from bioReservoirs to its connected downstream bioProcesses, and from these to their connected downstream bioReservoirs, moving along the bioModel's pathways. Inputs from external control systems or databases can be also forward-chained during run-time. A variety of methods are then used to compute or infer new values for the variables or parameters, derive conclusions and pass on control signals, and trigger action sequences, each as appropriate. The forward and backward associations between bioObjects for runtime execution are either inherent in the connections between the bioObjects or are explicitly configured through the model-blocks. The required integration of dataflow and sequential control mechanisms is accomplished in the currently preferred embodiment while taking advantage of the intuitive capabilities provided by the graphical architecture, where the bioObjects encapsulate the data to which related methods apply, and the parameters and variables are hidden but their values can be displayed. The specific way the bioObjects are connected specify both data flow and control flow, representing sequential or concurrent ordering of procedure execution, and the information needed to execute an algorithm is provided by or inferred from the architecture. The evaluation methods of the bioObjects involved in the simulated pathways execute in parallel during forward chaining, passing along the arguments to the posterior bioObjects, while the arguments of the anterior bioObjects are passed to them.

Paragraph [0149], at best, provides further description of the model of Thalhammer-Reyero but no teaching relating to claim 259 or Applicants' claimed methods. Applicants respectfully request that the Examiner provide guidance on what aspect of paragraph

[0149] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to paragraph [0589]:

> [0589] The simulation starts after a perturbation, such as a Concentration-Entry, Density-Entry or Scaled-Entry, has been introduced and integrated in the overall system's equation: d[E](t)/dt = [E](t) + entry + Σ inputs (t)-m*[E](t)-Σ outputs(t). In this system, the bioReservoirs and bioProcesses placed in a biological compartment-layer are activated successively in time and space, as the activation signal is propagating forwards based on various chaining relationships between those structures established during the initialization process according to the downstream or upstream positions of each of those structures respect to the others.

Paragraph [0589], at best, describes calculations related to the model of Thalhammer-Reyero but no teaching relating to claim 259 or to Applicants' claimed methods. Applicants respectfully request that the Examiner provide guidance on what aspect of paragraph [0589] is deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Referring to Figures 36a and b, this figure describes an example of pathways from multiple initial points (paragraph [0065] and is discussed in paragraph [0577], recited below:

> [0577] Selecting the PATHWAY button (**3520**) calls the draw-exper-pathway-callback (Table 227), which creates a navig-path-tracer (**3531**) together with its subworkspace by cloning the Master-Navig-Pathway and transfers it to the Panel, and then it scans the "Exper.Selections" list (**3512**) and for each bioReservoir listed calls the create-local-exper-BP-proc (Table 228), while setting the value of the x-pos to a value close to the initial position when changing from one bioReservoir to the next, which performs a processing very similar to that described earlier for the create-local-UBP-proc (Table 176) for the upstream direction. Now, instead of once as before, that procedure is called as many times as bioReservoirs are in the "Exper.Selections" list. One example of the display of one of those multi-origin pathways is shown in FIG. 36, which are more complex. The pathways start from multiple initial bioReservoirs, and the pathways from latter initial points are connected, whenever the possibility arises, to the pathways from former initial points already on the Experiment Pathway Display. Alternative implementations of any of the types of pathways are to include in the drawing of the pathways not only the bioProcesses, but also the bioReservoirs that are intermediaries between those process in the chaining process. The procedures for those alternative implementations (not shown) apply the same methods and

need only minor modifications to create, transfer and connect the intermediary bioReservoirs.

Thus, Figures 36a and b, at best, describe interconnected pathways but no teaching relating to claim 259 or Applicants' claimed methods. Applicants respectfully request that the Examiner provide guidance on what aspects of Figures 36a and b are deemed to support claim 259 of Thalhammer-Reyero so that Applicants can appropriately address the assertion.

Applicants respectfully maintain, for the reasons of record and as discussed above, that Thalhammer-Reyero provides no teaching of Applicants' claimed methods. Moreover, Applicants respectfully submit that much of the support set forth in the Office Action for the alleged anticipatory teachings of Thalhammer-Reyero cannot be afforded priority to the 102(e) date of Thalhammer-Reyero and therefore cannot anticipate Applicants' claimed methods. Accordingly, Applicants respectfully request that this rejection be withdrawn.

In light of the amendments and remarks herein, Applicants submit that the claims are now in condition for allowance and respectfully request a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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